REMARKS

Claims 1-10, 13-16, 26, and 28-32 are pending in the application.

Applicant notes that claims 28-34 were cancelled in the Preliminary Amendment filed February 6, 2001. However, in the Amendment and Response filed September 22, 2002, five new claims were added which were incorrectly numbered as beginning with number 28. Accordingly, claims 28-32 from the previous amendment have been renumbered as claims 35-39 herein.

Claims 2, 8, 13, and 35-39 have been amended herein to correct obvious typographical errors and for clarity. Accordingly, no new matter has been introduced by these amendments.

The specification has been amended herein to correct obvious typographical errors, to add "SEQ ID NO" designations, and to insert the sequence listing. Accordingly, no new matter has been introduced by these amendments.

Applicant respectfully requests that the Examiner return a copy of the first page of the 1449 submitted in the Information Disclosure Statement filed February 25, 2002 with the Examiner's initials indicating that references A1, A2 and A3 have been considered.

The outstanding rejections are addressed below.

1. Requirements for Sequence Listing

The specification was objected to because the application contained sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)1 and (a)2 but failed to comply with the requirements of 37 C.F.R. § 1.821 through 1.825.

Applicant encloses herewith a Sequence Listing in compliance with the requirements of 37 C.F.R. § 1.821 through 1.825. Applicant has also herein amended the specification to indicate SEQ ID NOS:1-2.

Accordingly, Applicant submits that this objection has been overcome and respectfully requests that the Examiner reconsider and withdraw this objection.

2. Rejection of claims 1-10, 13-16, 26, and 28-32 under 35 U.S.C. § 112, first paragraph

Claims 1-10, 13-16, 26 and 28-32 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement because the claims allegedly contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicant respectfully traverses this rejection.

The Office Action states that the specification on page 3 discloses references 6, 16, and 18-20 related to essential subject matter. The Office Action states on page 3 that Applicant is required to amend the disclosure to include the material incorporated by reference.

These five references, however, are merely cited following and in support of the statement at page 3, lines 12-15, that the "large majority of sporadic CJD cases are homozygous at polymorphic residue 129, a common protein polymorphism in human PrP that is known to play a key role in genetic susceptibility to human prion diseases." Thus, there is no "essential subject matter" contained in these references which is not already included in the specification, and the references are cited only to show that this information was well-known to those skilled in the art and available to the public.

For the Examiner's further consideration, the references in question are submitted herewith in connection with the Supplemental Information Disclosure Statement.

Applicant submits that review of the references in question will confirm that the references do not contain essential subject matter and, accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw this rejection.

3. Rejection of claims 1, 3-16, and 28-32 under 35 U.S.C. § 112, first paragraph

Claims 1, 3-16, and 28-32 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Applicant respectfully traverses this rejection.

In particular, the Office Action states that "[a]ll of the current claims encompass a genus of prion which are different from those disclosed in the specification [and that the] genus includes variants for which no written description is provided in the specification." (Office Action, page 4). The Office Action further states that "[i]n the application at the time of filing, there is no record or description which would demonstrate conception of any prions other than those expressly disclosed in the figures for examples. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification." (Office Action, page 5).

However, M.P.E.P. § 2163 (I) states that:

> To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention [at the time the application was filed]. . . .
>
> . . . Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" . . . or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention.

(Citations omitted.)

Therefore, at the outset, Applicant points out that the claimed embodiments of the invention in the rejected claims do not claim any genus of prions or, for that matter, prion sequences. Rather, the claims relate to methods for typing a sample of a prion or spongiform encephalopathy disease or methods of identifying infection in an animal and/or tissue of bovine spongiform encephalopathy. The claimed methods can, in fact, be performed on any PrP^{Sc} type, without prior knowledge of the amino acid sequences of the underlying prion proteins, and without prior knowledge of the particular physicochemical properties of the prion types.

Indeed, contrary to the suggestion in the Office Action, Applicant has shown possession of the invention by providing a written description of how to practice the methods of the invention for any prion types having different physicochemical properties. In addition, the specification illustrates the practice of the invention with a number of different prion types. Thus, Example 3 describes that "[s]amples from 100 CJD patients were PrP^{Sc} typed according to the methods already described above" and that two new distinct patterns of protease resistant PrP (named types 6 and 7) were identified. (Page 28, lines 15-18). Thus, the claimed methods were specifically shown to work with known prion types and to be able to identify new PrP^{Sc} types. Furthermore, the specification discloses seven different PrP^{Sc} "types" in the application as filed. Types 1 and 2 are discussed at, *inter alia*, page 8 of the specification. Type 3 is discussed at, *inter alia*, page 9 of the specification. Type 4 is discussed at, *inter alia*, page 19 of the specification. Type 5 is discussed at, *inter alia*, page 26 of the specification. Types 6 and 7 are described at page 28 and Figure 9 of the specification. In contrast, the Office Action provides no evidence or reasoning indicating that the claimed methods could not be performed on these or any other prion types.

Moreover, Applicant submits that the specification teaches at page 14, line 20 to page 15, line 4, that the claimed invention does depend on knowledge of the gene or protein sequences:

> The finding that strains appear to involve different post-translational modifications of PrP which persist or (when PrP genotypes are mismatched) can be predictably converted between discrete strains on passage in mice is consistent with a "protein only" model of prion propagation in which strains are encoded by post-translational modification of PrP itself without the need for nucleic acid or other co-factor. The bands seen on Western analysis of PrP following proteolytic cleavage represent diglycosylated, monoglycosylated (at either of the two N linked glycoslyation sites[34]) and unglycosylated PrP, and two separate features of these bands, shifts in mobility and differences in relative intensities, appear to be associated with strain type. The mobility shifts after cleavage, seen in all three bands, imply different PrP conformations (which may include differing states of assembly). The differences in glycoform ratios could indicate preferential conversion of particular glycoforms into particular conformational states. (emphasis added)

Thus, it is the physicochemical properties, in particular the sizes and ratios of distinct PrP^{Sc} glycoforms, that are being compared and identified in the claimed embodiments of the invention.

Furthermore, with regard to claim 13, the claim specifies that the infection is bovine spongiform encephalopathy. Examples of the specific banding pattern for bovine spongiform encephalopathy are provided in the specification. It is merely necessary to identify that the isolated prion protein has the specific banding pattern described or has substantially similar glycoform proportions as bovine spongiform encephalopathy.

Accordingly, because Applicant has claimed methods of typing samples and methods of identifying infections rather than prion proteins themselves, because

Applicant has disclosed several examples of the practice of the methods with different PrP^{Sc} "types", and because there is no evidence of record which indicates that the invention would not work with other prion types, Applicant submits that the specification shows that the inventor was in possession of the invention as claimed in view of the disclosure of the application as filed.

Finally, Applicant respectfully submits that the assertion in the Office Action that the claims are directed to a genus which "comprises hundreds of millions of different possibilities" is unsupported. (Office Action, page 4). The Office Action provides no reason for supposing that the "genus" of prion types encompasses so many species. Thus, if this rejection is to be maintained, Applicant respectfully requests the Examiner to provide her own affidavit, pursuant to 37 C.F.R. §1.104(d)(2), in support of this statement.

For the foregoing reasons, Applicant submits that the rejection under 35 U.S.C. § 112, first paragraph has been overcome, and respectfully requests that this rejection be reconsidered and withdrawn.

4. Rejection of claims 1-10, 13-16, and 28-30 under 35 U.S.C. § 102(a) over Parchi *et al.*

Claims 1-10, 13-16, and 28-30 stand rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Parchi *et al.* Applicant respectfully traverses this rejection.

M.P.E.P. 2131 provides that:

> "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). . . . "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim . . . .

With regard to claim 1, and claims dependent thereon, Applicant submits that Parchi *et al.* does not disclose the step of comparing and identifying similar physicochemical properties (sizes and ratios of distinct PrP^{Sc} glycoforms) of the sample *with a standard sample of known PrP^{Sc} type* in order to type an unknown sample of a prion or spongiform encephalopathy disease. Parchi *et al.* in Figure 1 compare type 1 and type 2 PrP^{res} to each other but they do not specifically compare the sizes and ratios of distinct PrP^{Sc} glycoforms of a sample with a standard sample of known PrP^{Sc} type in order to type an unknown sample. Thus, Parchi *et al.* does not disclose each and every element of claim 1 and cannot be held to anticipate the claim.

In addition, with regard to claim 13, and claims dependent thereon, Applicant submits that Parchi *et al.* relates only to CJD and does not disclose the specific banding pattern resulting from bovine spongiform encephalopathy.

Specifically, claim 13 relates to a method of identifying infection in an animal and/or tissue of bovine spongiform encephalopathy. The method comprises isolating a prion protein from the animal and/or tissue and identifying that said prion protein can be characterized by having three distinct bands on an electrophoresis gel following proteinase K digestion. The bands comprise (i) a band of highest molecular weight *in the greatest proportion*, (ii) a band of lowest molecular weight *in the lowest proportion*, and (iii) a band with a molecular weight between the bands of (i) and (ii) and a *proportion between the bands of (i) and (ii)* or characterized by having substantially similar glycoform proportions as bovine spongiform encephalopathy.

In contrast, Parchi *et al.* does not disclose that prion proteins derived from a BSE-infected sample will have the physicochemical properties recited in claim 13. Rather, Parchi *et al.* characterizes types 1 and 2 of CJD, which do not have the glycoform ratios of BSE, as recited in claim 13. For example, Table 1 of Parchi *et al.* indicates that the medium size glycoform ("lower glycoform" in Table 1) of both types 1 and 2 is shown

to be present in the highest proportion. Therefore, types 1 and 2 CJD do not show the same banding pattern as BSE.

Thus, Parchi *et al.* does not disclose each and every element of claim 13 and cannot be held to anticipate the claim.

Accordingly, Applicant submits that claims 1-10, 13-16, and 28-30 are not anticipated by Parchi *et al.*, and Applicant respectfully requests that these rejections be reconsidered and withdrawn.

CONCLUSIONS

In view of the arguments set forth above, Applicant respectfully submits that the rejections contained in the Office Action mailed on June 29, 2004, have been overcome, and that the claims are in condition for allowance. If the Examiner believes that any further discussion of this communication would be helpful, she is invited to contact the undersigned at the telephone number provided below.

Applicant encloses herewith a petition for a three month extension of time until December 29, 2004 to respond to the Office Action dated June 29, 2004. Please charge our Deposit Account No. 08-0219 the $1020.00 fee for this extension of time.

Applicant also encloses herewith a Supplemental Information Disclosure Statement. Please charge our Deposit Account No. 08-0219 the $180.00 fee for this purpose.

No other fees are believed to be due in connection with this response. However, please charge any underpayments or credit any overpayments to Deposit Account No. 08-0219.

Respectfully submitted,

Michael J. Twomey
Reg. No. 38,349

Date: December 29, 2004
WILMER CUTLER PICKERING
HALE AND DORR LLP
60 State Street
Boston, MA 02109
Tel: (617) 526-6190
Fax: (617) 526-5000